

What is claimed is:

1. Method for inducing or preventing the apoptosis of eukaryotic cells comprising the homing on specific tissue cell population of a chimeric bifunctional molecule able to modulate the activity of permeability transition pore complex (PTPC).
2. A method according to claim 1, wherein said chimeric molecules modulate the activity of the permeability transition pore complex (PTPC) of a specific eukaryotic cell by the regulation of opening or the closing of said pore.
3. A method according to claim 1 or 2, wherein said chimeric molecules comprising at least a first functional molecule and a second functional molecule, wherein said first functional molecule has the function to target specifically a tissue cell population, and the second functional molecule has the function to regulate the apoptosis activity linked to the permeability transition pore complex (PTPC) of said specific cells.
4. A method according to claim 3, wherein said chimeric molecules comprising at least a first functional molecule and a second functional molecule, wherein said first functional molecule has the function to target and to enter specifically in a tissue cell population and the second functional molecule has the function to regulate the apoptosis activity linked to the permeability transition pore complex (PTPC) of said specific cells.
5. A method according to claim 3, wherein said chimeric molecules comprising at least a first functional molecule and a second functional molecule, wherein said first functional molecule has the function to target and to enter specifically in a tissue cell population of interest and the second functional molecule has the function to target specifically and inducing or preventing the death of said cells by apoptosis by the regulation of the

opening or the closing of the permeability transition pore complex (PTPC) of mitochondria or a fragment thereof.

6. A method according to claim 4, wherein said chimeric molecule has the formula:

Targ-Tox,

wherein Tox is a viral or a retroviral apoptotic peptide or a peptidomimetic or a fragment of a protein that interacts with permeability transition pore complex (PTPC) of a specific eukaryotic cell to cause apoptosis of the cell; and Targ is chosen from:

an antibody,

an antibody fragment,

arecombinant antibody fragment,

M350/ScFv,

V461/ScFv,

a homing peptide, and

any peptide chosen in Table III,

wherein said molecule binds and enters the cell specifically.

7. A method according to claim 5, wherein said chimeric molecule has the formula

Targ-Save,

wherein Save is a viral or a retroviral or a cellular antiapoptotic peptide or peptidomimetic or a fragment of protein that interacts with permeability transition pore complex (PTPC) of a specific eukaryotic cell to prevent the apoptosis of the cell with the proviso that when Save peptide is a viral peptide, Save is not vMIA protein of Cytomegalovirus; and

Targ is chosen from:

an antibody,

an antibody fragment,

a recombinant antibody fragment,

M350/ScFv,

a homing peptide, and

any peptide chosen in Table III,

wherein said molecule binds and enters the cell specifically.

8. A method according to anyone of claims 1 to 7, wherein said chimeric molecules comprises a Mitochondrial Localisation Sequence (MLS), which has the function to address specifically the second functional molecule to mitochondrial or intermembrane space-of the mitochondria.
9. A method according to claims 1, 2, 3, 4, 5, 6 and 8, wherein Tox is chosen from the group of peptides of Table I.
10. A method according to claims 1, 2, 3, 4, 5, and 7, wherein Save is chosen from the group of peptides of Table II.
11. A method according to any one of claims 1 to 10, wherein the second functional molecule of said chimeric molecules has the function to interact specifically with ANT of the PTPC of mitochondria also refers to as adenine nucleotide translocator isoforms 1, 2, or 3.
12. A chimeric bifunctional molecule capable to enter specifically in a tissue cell population for induce or prevent death of said cell by apoptosis and comprising at least a first functional molecule covalently linked to a second functional molecule, wherein said first

functional molecule has the function to target and to enter specifically in a tissue cell population of interest and the second functional molecule has the function to target specifically and inducing or preventing the death of said cells by apoptosis by the regulation of the opening or the closing of the permeability transition pore complex (PTPC) of mitochondria or a fragment thereof.

13. A chimeric molecule according to claim 12 which has the formula:

Targ-Tox,

wherein Tox is a viral or a retroviral apoptotic peptide or peptidomimetic or a fragment of a protein that interacts with PermeabilityTransifion Pore Complex (PTPC) of a specific eukaryofic cell to cause apoptosis of the cell; and

Targ is chosen from:

an antibody,

an antibody fragment,

a recombinant antibody fragment,

M350/ScFv,

V461/ScFv,

a homing peptide, and

any peptide of Table III,

wherein said molecule binds and enters the cell specifically.

14. A chimeric molecule according to claim 12 which has of the formula

Targ-Save

Wherein Save is a viral or a retroviral or a cellular antiapoptotic peptide or peptidomimetic or a fragment of protein that interacts with Permeability Transition Pore Complex (PTPC) of a specific eukaryotic cell to prevent apoptosis of the cell, with the proviso that when Save peptide is a viral peptide, Save is not vMLA protein of Cytomegalovirus;

and Targ is chosen from:

an antibody,

an antibody fragment,

a recombinant antibody fragment,

M350/ScFv,

a homing peptide, and

any peptide of Table III,

wherein said molecule binds and enters the cell specifically.

15. A chimeric molecule according to any of claims 12 to 14 comprising a mitochondrial localisation sequence (MLS) which has the function to address specifically the second functional molecule to mitochondrial membranes or intermembrane space.
16. A chimeric molecule according to claims 13 or 15, wherein Tox is chosen from the group of peptides of Table I.
17. A chimeric molecule according to claims 14 and 15, wherein wherein Save is chosen from the group of peptides of Table II.
18. A chimeric molecule according to claims 13, 15 and 16, wherein the Targ and Tox peptides are covalently bonded through a peptide linker comprising 3 to 18 amino acids.

19. A chimeric molecule according to claims 14, 15 and 17, wherein the Targ and Save peptides are covalently bonded through a peptide linker comprising 3 to 18 amino acids.
20. A vector encoding a chimeric molecule as claimed in any one of claims 12 to 19.
21. A hybridoma secreting Targ according to claim 13 or 14 and deposited at the National Collection of Culture and Microorganism (C.N.C.M.) on January 24, 2001, under the accession number n° I 2617.
22. A purified monoclonal antibody encoded by the hybridoma of claim 21.
23. A recombinant host cell comprising a vector as claimed in claim 20.
24. A cancer cell having a tumor associated antigen on the surface thereof to which is bound the chimeric molecule as claimed in any one of claims 12 to 19.
25. A method of determining the presence of a cancer cell having a tumor-associated antigen on the surface thereof in a biological sample comprising :
  - a) contacting a biological sample of interest with a chimeric peptide molecule according to claims 12 to 19 under conditions to permit the binding between the chimeric peptide according to the invention and the antigen on the surface of the cancer cell,
  - b) detecting the binding by usual technique; and
  - c) optionally quantifying the binding detected in step b).
26. A method for inducing death by apoptosis in a tumoral or viral infected cell having a tumor-associated antigen on surface thereof in a biological sample comprising:  
contacting a biological sample of interest with a chimeric peptide molecule according to claims 16 or 17 under conditions to permit the binding between the chimeric peptide

according to the invention and the antigen on the surface of the cancer cell and for a time sufficient to allow the entry inside the cell and death cell by apoptosis or viral infected cells.

27. A method for prevent cell death by mitochondrial apoptosis comprising contacting a biological sample of interest with a chimeric molecule, **molecule** according to claims 17 or 19 under conditions to permit the binding between the chimeric molecule according to the invention and the cell of interest and for a time sufficient to allow the entry inside cell of interest and prevent the cell death by apoptosis.
28. A method for prevent cell death according to claim 27, wherein the cells of interest are choosen among the following cell populations: neurons, cardiocytes, and hepatocytes.
29. A method for identifying an active agent of interest that interacts with the activity of the permeability transition pore complex (PTPC) comprising
- a) contacting a biological sample containing cells with permeability transition pore complex (PTPC) with a chimeric peptide according to claims 12 to 19 in the presence of a candidate agent; and
  - b) comparing the binding of the chimeric peptide with the permeability transition pore complex (PTPC) in absence of said agent.
  - c) optionally, testing the activity of said selected agent on a preparation of a cellular extract comprising subcellular elements with the permeability transition pore complex (PTPC).

30. A method for identifying an active agent of interest that interacts with ANT peptide of permeability transition pore complex (PTPC) comprising:
- d) contacting a biological sample containing cells with ANT peptide of permeability transition pore complex (PTPC) with a chimeric peptide according to claims 12 to 19 in the presence of a candidate agent; and
  - e) comparing the binding of the chimeric peptide with the ANT peptide of the permeability transition pore complex (PTPC) in absence of said agent.
  - f) optionally, testing the activity of said selected agent on a preparation of a cellular extract comprising subcellular elements with the ANT peptide of the permeability transition pore complex (PTPC).
31. A method of identification of mitochondrial antigen, said antigen having the capacity to interact with a macromolecule or a molecule or a peptide carrying the characteristic of Tox according to claims 13 or 16.
32. A method of identification of mitochondrial antigen, said antigen having the capacity to interact with a macromolecule or a molecule or a peptide carrying the characteristic of save according to claims 14 or 17.
33. A method of treatment or of prevention of a pathological infection or disease comprising the administration to a patient of the pharmaceutical composition containing at least a chimeric molecule according to any of claims 12 to 19.
34. A pharmaceutical composition comprising at least a chimeric molecule according to claims any of 12 to 19.